Annals of Clinical and Analytical Medicine
Original Research

Evaluation of patients who had lumbar puncture in the emergency department

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Abstract

Aim: In our study, it was aimed to contribute to the literature by investigating the clinical characteristics, predisposing factors, causative microorganisms and mortality rates of the patients followed up with the diagnosis of community-acquired CNS infection.

Material and Methods: Demographic data, clinical findings, and laboratory values of patients older than 18 years of age who applied to the emergency medical clinic of the hospital and were diagnosed with CNS infection were collected from their medical records. Persons under the age of 18 who were transferred to another health center, diagnosed with nosocomial CNS infection were excluded from the study

Results: Of the 46 patients included in the study, 56.5% were female and 43.5% were male. It was observed that the mean age of the patients was 51.5±2.4. Of the patients, 45.65% had acute bacterial meningitis, 34.78% had encephalitis-aseptic meningitis, 8.69% had tuberculous meningitis, 6.52% had fungal meningitis, and 4.34% had brain abscess. When the patients were evaluated according to their physical examination and hospital admission complaints, in the patients with acute bacterial meningitis, fever was present in 76.19%, altered consciousness in 71.42% , headache in 66.6% , and CNS irritation findings in 66.6%. Aseptic meningitis/encephalitis patients had altered consciousness in 75%, headache in 62.5%, and fever in 56.25%. When the predisposing factors in patients with fungal meningitis were evaluated, it was observed that 66.6% of the patients and 50% of the patients with tuberculous meningitis had an immunosuppressive condition. There was no growth in CSF culture in 38.09% of acute bacterial meningitis patients. No causative agent was detected in 43.75% of aseptic meningitis-encephalitis patients. Varicella Zoster Virus (VZV) was the most common causative agent in aseptic meningitis-encephalitis patients. Neurological deficit developed as a complication in 30.09% of patients with acute bacterial meningitis, in 25% of patients with aseptic meningitis-encephalitis, in 50% of patients with tuberculous meningitis, in 33.3% of patients with fungal meningitis and in 50% of patients with brain abscess.

Discussion: Clinic and prognosis of CNS infections differ according to the age of the patient, the causative microorganism, the time of diagnosis and initiation of treatment, and predisposing factors such as conditions causing immunosuppression. In our study, contrary to much literature, VZV was most commonly isolated in patients with aseptic meningitis-encephalitis. It should also be kept in mind that there may not be a risk factor in cases of CNS infection. Complications should be closely monitored in patients with acute bacterial meningitis, brain abscess, and tuberculous meningitis.

Keywords

CNS Infection, Emergency Medicine Clinic, Lumbar Puncture

DOI: 10.4328/ACAM.21516 Received: 2022-11-24 Accepted: 2023-01-05 Published Online: 2023-01-09 Printed: 2023-03-01 Ann Clin Anal Med 2023;14(3):212-217
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This study was approved by the Clinical Research Ethics Committee of Harran University (Date: 2021-06-21, No: HRU/12.12.14)

Introduction

Central nervous system (CNS) infections are infections of the brain meninges and/or brain parenchyma due to bacteria, viruses, and fungal agents. Clinically, It may present with changes in consciousness, headache, fever, nausea, vomiting, and focal neurological findings. Depending on the type of infection, it can be acute, subacute, or chronic, as well as self-limiting or rapidly spreading types [1].

Etiological factors vary depending on age, geographical differences, seasonal periods, susceptibility of communities to certain factors, other diseases, genetic structure, socioeconomic conditions, and local endemic factors [2]. Poverty due to socioeconomic conditions, crowded common living areas, difficulties in accessing health services, and low education level of parents are other important factors that increase the frequency of CNS infections [3]. Although advanced diagnostic methods are used to isolate the factors, the etiologic agent cannot be determined in 32-75% of the patients [4].

Streptococcus pneumonia is the most common cause of acute bacterial meningitis. The most common factor in aseptic meningitis is enteroviruses [5]. Herpes Simplex Virus (HSV) stands out as another important factor in aseptic meningitis [6].

Early diagnosis and effective treatment in patients with CNS infection have an important place in the survival of patients. In acute bacterial meningitis, lumbar puncture (LP) should be performed without wasting time, and bactericidal antibiotics should be started, which pass into the CNS according to cerebrospinal fluid (CSF) gram staining results. In cases where the Gram staining result is negative or LP cannot be performed, empirical treatment should be started considering the patient's age and clinic [7]. It is difficult to distinguish between bacterial and viral infections in the diagnosis of central nervous system infections. It was observed that in 21.4% of the patients, empiric antibacterial and antiviral treatments were given together [8].

Our study, it was aimed to contribute to the literature by investigating the clinical characteristics, predisposing factors, causative microorganisms and mortality rates of the patients followed up with the diagnosis of community-acquired CNS infection.

Material and Methods

In our study, the files of the patients who applied to Şanlıurfa Training and Research Hospital Emergency Medicine Clinic in 2019-2021, who had LP in the emergency room red area, and were admitted to the Infectious Diseases Clinic with the diagnosis of CNS infection were retrospectively examined. Ethics committee approval of the study was received from Harran University Clinical Research Ethics Committee (Decision Date: 21.06.2021, Decision No: HRU/12.12.14).

Demographic data, clinical findings, and laboratory values of patients older than 18 years of age who applied to the emergency medical clinic of the hospital and were diagnosed with CNS infection were collected from their medical records. Persons under the age of 18 who were transferred to another health center and diagnosed with nosocomial CNS infection were excluded from the study.

Chronic otitis-sinusitis, splenectomy, previous cranial operation history, and immunosuppressive conditions were accepted as predisposing factors. Severe malnutrition due to alcohol dependence, malignancy, anorexia nervosa, HIV positivity, and immunosuppressive drug use were evaluated under the name of the immunosuppressive condition.

CNS infection classification was classified according to the clinical findings of the patients, the findings in the CSF evaluation (CSF Protein level, dominant cell type, CSF gram staining, Indian ink staining and culture, CSF Polymerase Chain Reaction (PCR) examination, CSF glucose levels, and CSF/blood glucose ratios) and cranial imaging findings. Patients were grouped as acute bacterial meningitis, aseptic meningitis-encephalitis, tuberculous meningitis, brain abscess, and fungal meningitis.

Abscess and CSF samples were seeded on Eosin Methylene Blue agar, chocolate agar, and blood agar. These samples were incubated at 37°C for 24-48 hours. CSFs of suspected cases of cryptococcal meningitis were evaluated with Indian ink dye. Sabouraud dextrose agar medium was used for the detection of fungal agents.

Automatic (VITEK 2, Automatic ID/ADT tester,) methods were used to identify bacteria that grew at the end of incubation. HSV1, HSV2, VZV, and "Enterovirus, Parechovirus multiplex PCR" were studied in the viral meningitis panel. Real-time PCR and conventional culture methods were used for Mycobacterium tuberculosis.

Information such as patients' complaints at admission, predisposing factors, examination findings and CSF findings, complications, and mortality rates were evaluated.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

Of the 46 patients included in the study, 56.5% were female (n=26) and 43.5% (n=20) were male. It was observed that the mean age of the patients was 51.5±2.4 years.

Of the patients, 45.65% (n=21) had acute bacterial meningitis, 34.78% (n=16) had encephalitis-aseptic meningitis, 8.69% (n=4) had tuberculous meningitis, 6.52% (n=3) had fungal meningitis, and 4.34% (n=2) had brain abscess.

When the patients were evaluated according to their physical examination and hospital admission complaints, among the patients with acute bacterial meningitis, fever was present in 76.19%, altered consciousness in 71.42%, headache in 66.6%, and CNS irritation findings in 66.6% (nuchal stiffness, Brudzinski and Kerning findings), 57.14% had nausea-vomiting and 23.8% had epileptic seizures. Among patients with aseptic meningitis/encephalitis, 75% had consciousness changes, 62.5% had headache, 56.25% had fever, 50% had nausea-vomiting, 37.5% had CNS irritation findings and 18.75% had epileptic seizures. Among patients with tuberculous meningitis, 75% had fever, 75% had headache , 75% had CNS irritation findings, 50% had nausea-vomiting and 50% of them had complaints of altered consciousness. Among patients with fungal meningitis, 100% had headache, 100% had nausea-vomiting, 66.6% had fever, 33.3% had altered consciousness, and 33.3% of them had CNS irritation findings. It was observed that all patients with brain abscess had fever, headache and nausea-vomiting, while half of

Table 1. Application complaints and physical examination findings of patients diagnosed with CNS infection

Complaints and Physical Examination Findings	Acute Bacterial Meningitis (n=21)	Aseptic Meningitis Encephalitis (n=16)	Tuberculous Meningitis (n=4)	Fungal Meningitis (n=3)	Brain Abscess (n=2)
Fever	%76.19	%56.25	75%	%66.6	100%
Headache	%66.6	%62.5	75%	100%	100%
CNS Irritation Findings (Neck stiffness, Brudzinski and Kerning findings)	%66.6	%37.5	75%	%33.3	50%
Consciousness change	%71.42	75%	50%	%33.3	50%
Nausea-vomiting	%57.14	50%	50%	100%	100%
Epileptic seizure	%23.8	%18.75	-	-	50%

Table 2. Laboratory findings of patients diagnosed with CNS infection

	Acute Bacterial Meningitis (n=21)	Aseptic Meningitis Encephalitis (n=16)	Tuberculous Meningitis (n=4)	Fungal Meningitis (n=3)	Brain Abscess (n=2)
CSF mean protein (15-45 mg/dL)	333±52 mg/dL	132±34 mg/dL	474±66 mg/dL	178±24 mg/dL	-
CSF mean cell (mm3)	4872	176	167	182	-
CSF glucose*	%80.95 (n=17)	%56.25 (n=9)	75% (n=3)	100% (n=3)	-

*Patients with concomitant CSF glucose of less than one-third of blood glucose

Table 3. Agents detected by culture or polymerase chain reaction (PCR)

	Detected Factor	% (n)
Acute bacterial meningitis (n=21)	Streptococcus pneumoniae	%23.8
	Neisseria meningitidis	%14.28
	Coagulase Negative Staphylococcus	%9.5
	Escherichia coli	%9.5
	Listeria Monocytogenes	%4.76
	Varicella Zoster Virus (VZV)	%31.25
Aseptic meningitis-encephalitis (n=16)	HSV-1	%12.5
	HSV-2	%12.5
Tuberculous meningitis (n=4)	Mycobacterium tuberculosis (Culture positive)	75%
	Mycobacterium tuberculosis PCR positive	25%
Fungal meningitis (n=3)	Cryptococcus neoformans	100%
Brain abscess (n=2)	Nocardia spp.	50%

the patients had epileptic seizures, CNS irritation findings and changes in consciousness (Table 1).

The mean age of acute bacterial meningitis patients was 46.52 ± 9.1 years. Of these patients, 52.38% were female and 47.62% were male. When the predisposing factors were evaluated, 28.57% of acute bacterial meningitis patients had chronic sinusitis, 19.04% had a history of previous cranial operation, 14.28% had immunosuppression and in 4.76% of patients, chronic otitis was observed. The mean age of aseptic meningitis/encephalitis patients was 56.56 ± 6.4 years. 56.25% of the patients were female and 43.75% were male. When the predisposing factors were evaluated, splenectomy was observed in 12.5% of the patients, immunosuppression status was observed in 12.5%, chronic otitis was observed in 6.25% and chronic sinusitis was observed in 6.25%. The mean age of patients with tuberculous meningitis was 40.5 years. 75% of the patients were female and 25% were male. When the predisposing factors were evaluated, it was observed that 50% of the patients had an immunosuppressive condition. The mean age of patients with fungal meningitis was 73.33 years. 66.6% of the patients were female and 33.3% were male. When the predisposing factors were evaluated, it was observed that 66.6% of the patients had a condition that caused immunosuppression. The mean age of patients with brain abscesses was 53.5 years. 50% of the patients were male and 50% were female. When the predisposing factors were evaluated, it was observed that 50% of the patients had chronic sinusitis and 50% had chronic otitis.

In the laboratory findings of acute bacterial meningitis patients, the mean amount of CSF protein was found to be 333±52 mg/dL and the mean CSF cell count was 4872 mm3. In 80.95% of the patients, CSF glucose was found to be lower than one-third of concurrent serum blood glucose. In the laboratory findings of aseptic meningitis/encephalitis patients, the mean amount of CSF protein was 132±34 mg/dL and the mean CSF cell count was 176 mm3. In 56.25% of the patients, CSF glucose was found to be lower than one-third of concurrent serum blood glucose. In the laboratory findings of patients with tuberculous meningitis, the mean amount of CSF protein was 474±66 mg/dL and the mean CSF cell count was 167 mm3. In 75% of the patients, CSF glucose was found to be lower than one-third of concurrent serum blood glucose. In the laboratory findings of patients with fungal meningitis, the mean amount of CSF protein was found to be 178±24 mg/dL and the mean cell count of CSF was 182 mm3. In 100% of the patients, CSF glucose was found to be lower than one-third of concurrent serum blood glucose (Table 2).

There was no growth in CSF culture in 38.09% of acute bacterial meningitis patients. 23.8% of these patients grew Streptococcus Pneumoniae, 14.28% of these patients grew Neisseria Meningitidis, 9.5% of these patients grew Coagulase Negative Staphylococci, 9.5% of these patients were grew Escherichia Coli and 4.76% of these patients grew Listeria Monocytogenes. No causative agent was detected in 43.75% of

aseptic meningitis-encephalitis patients. Varicella Zoster Virus (VZV) in 31.25%, HSV-1 in 12.5%, and HSV-2 in 12.5% of the patients, by PCR were detected. Mycobacterium tuberculosis culture positive was found in 75% of patients with tuberculous meningitis and Mycobacterium tuberculosis PCR positive in 25%. Cryptococcus neoformans was detected in CSF Indian ink staining in all patients with fungal meningitis. There was no growth in the abscess culture in 50% of the patients with brain abscesses. Nocardia spp was detected in 50% of the patients (Table 3).

When the patient group with acute bacterial meningitis was evaluated in terms of complications, it was observed that 30.09% had neurological deficits, 9.5% had hydrocephalus, 9.5% had epileptic seizures and 4.76% developed inappropriate ADH syndrome. Neurological deficits were observed in 25% of patients with aseptic meningitis-encephalitis, Inappropriate ADH Syndrome was observed in 6.25%, and epileptic seizures was observed in 6.25%. It was observed that 50% of the patients with tuberculous meningitis developed neurological deficits and 25% developed hydrocephalus. Neurological deficit was observed in 33.3% of patients with fungal meningitis. It has been observed that 50% of patients with brain abscesses develop hydrocephalus and neurologic deficits.

The outcome of three patients with acute bacterial meningitis, two patients with aseptic meningitis-encephalitis, one patient with tuberculous meningitis and one patient with fungal meningitis resulted in death.

Discussion

Despite the antimicrobial treatment protocols and vaccines developed in recent years, meningitis continues to be a public health problem with high morbidity and mortality [9]. CNS infections are infectious diseases that can result in permanent damage or death in cases where early diagnosis and treatment cannot be applied. CNS infections can be seen in many different clinical forms such as acute bacterial meningitis, acute viral meningitis, chronic meningitis, brain abscesses, and encephalitis. When sorted according to clinical classifications, the most common disease is acute bacterial and viral meningitis [7]. Acute bacterial and viral meningitis are the most frequently detected clinical manifestations [10]. In our study, acute bacterial and viral meningitis was observed as the most common clinical picture with a rate of 80.43%.

Trauma, malignancy, splenectomy, use of immunosuppressive drugs, organ transplantation, alcohol dependence, and high-dose steroid therapy are the underlying risk factors for the development of acute bacterial meningitis [7]. In one study, head trauma and chronic otitis media were identified as the most common predisposing factors in the development of acute bacterial meningitis [11]. In our study, the most common predisposing factors were found to be chronic sinusitis and a history of previous cranial surgery.

Brain abscess may develop because of paranasal sinusitis, otitis media, cyanotic heart diseases, bacterial endocarditis, pneumonia, lung abscess, penetrating head trauma, post neurosurgery, and conditions that cause immunosuppression [12]. When the predisposing factors of the patients diagnosed with brain abscesses were evaluated in our study, it was observed that 50% of the patients had chronic sinusitis and 50% had chronic otitis. Therefore, we think it is important to question the predisposing factors in patients.

One of the most prominent predisposing factors for cryptococcal meningitis is acquired immunodeficiency syndrome [10]. In a multicenter study, no underlying risk factor was found in 30% of the patients [13]. In our study, no underlying risk factor was found in 33.33% of the patients diagnosed with fungal meningitis.

The most common symptoms of fever, CNS irritation, and altered consciousness were found in patients diagnosed with acute bacterial meningitis [14, 15]. In our study, it was observed that 76.19% of the patients with acute bacterial meningitis had fever, 71.42% had altered consciousness, 66.6% had headache, and 66.6% had CNS irritation findings.

In a multicenter study, it was reported that 72% of encephalitis patients developed fever, 60% headache, and 23% CNS irritation findings [16]. In our study, it was observed that 75% of aseptic meningitis/encephalitis patients had changes in consciousness, 62.5% had headache and 56.25% had fever.

In a study evaluating cases with tuberculous meningitis, it was found that 75% of the patients had fever, 63% had a change in consciousness, 38% had headache, and 25% had CNS irritation [15]. In another study, it was observed that more than 80% of the patients had a fever, headache, and CNS irritation findings [17]. In our study, it was observed that 75% of the patients with tuberculous meningitis had fever, headache, and CNS irritation findings. The differences in these rates were thought to be because of the single-center nature of our study and the relatively low number of patients.

The rate of causative isolation in acute bacterial meningitis was found to be 35% in a study, and 28% in aseptic meningitis-encephalitis patients [15]. In our study, the agent could not be isolated in 38.09% of the patients. In one study, it was observed that the factor identification rate in encephalitis was between 38-63% [18]. It is thought that the detection rate of viral agents will increase with the use of advanced molecular tests. In our study, no causative agent was detected in 43.75% of aseptic meningitis-encephalitis patients.

Mycobacterium tuberculosis culture was positive in 75% of patients with tuberculous meningitis and Mycobacterium tuberculosis PCR was positive in 25%. Our rate of detecting the causative agent in patients with tuberculous meningitis was found to be higher than in the literature [19].

Although factors vary according to age in patients with bacterial meningitis, the most common cause is S.pneumoniae. In elderly patients, E.coli and L.monocytogenes may be the cause [20,21]. In our study, Streptococcus Pneumoniae (23.8%) and Neisseria Meningitidis (14.28%) were the most frequently isolated agents in patients. It has been observed that our findings are compatible with the literature.

Enteroviruses are the most common cause of aseptic meningitis, but HSV is another important virus group [6]. In another study, VZV was most frequently isolated in patients with aseptic meningitis/encephalitis [15]. In our study, VZV was detected in 31.25% of the patients, HSV-1 in 12.5% , and HSV-2 in 12.5% of the patients. This suggests that VZV should also be considered in the etiology of aseptic meningitis-encephalitis.

A pyogenic brain abscess is usually a mixed infection with commonly found anaerobic organisms. Staphylococci, streptococci, and Enterobacteriaceae are common aerobic pathogens. Nocardia, Listeria, and Pseudomonas are not rarely isolated in immunosuppressed patients [12]. In our study, there was no growth in the abscess culture in 50% of the patients diagnosed with brain abscesses. Nocardia spp was detected in 50% of the patients.

Complications such as hydrocephalus, cerebral edema, seizures, and cerebral infarction may be encountered in patients with CNS infection [18]. In a study conducted on patients with acute bacterial meningitis, the complication rate was found to be 6.5% [20]. In another study, it was observed that complications developed at a rate of 29%. [15]. In our study, this rate was found to be 53.89%. It was found to be high according to the literature.

In a study including patients with tuberculous meningitis, neurological sequelae developed in 22% of patients [19]. In another study, 19.4% of patients developed neurological sequelae, 13.9% had inappropriate ADH syndrome, and 50% developed hydrocephalus. [17]. Again, in a different study conducted in this patient group, it was found that 38% of the patients had neurological sequelae and 13% had hydrocephalus [15]. In our study, it was observed that 50% of the patients with tuberculous meningitis developed neurological deficits, and 25% developed hydrocephalus.

Mortality of CNS infections is associated with early diagnosis and initiation of treatment with advanced diagnostic molecular methods. When evaluated according to clinical classifications, mortality rates in the acute bacterial meningitis patient group were found to be between 10%-13.6% [10, 15, 20]. In our study, it was observed that the mortality rate was 14.28% in patients diagnosed with acute bacterial meningitis.

In various studies conducted in our country, mortality rates in patients diagnosed with tuberculous meningitis were found to be 10-47% [1, 5, 15, 19]. In our study, the mortality rate of patients with tuberculous meningitis was observed to be 25%.

In one study, the mortality rate was found to be 25% in the fungal meningitis patient group [15]. In our study, the mortality rate in patients with fungal meningitis was found to be 33.3%. This high rate was attributed to the high mean age of the patients and immunosuppression in 66.6% of the patients.

Conclusion

Clinic and prognosis of CNS infections differ according to the age of the patient, the causative microorganism, the time of diagnosis and initiation of treatment, and predisposing factors such as conditions causing immunosuppression. It should also be kept in mind that there may not be a risk factor in cases of CNS infection. Complications should be closely monitored in patients with acute bacterial meningitis, brain abscess, and tuberculous meningitis. Knowing the distribution of the factors causing CNS infections and the predisposing factors is important in the management of patients and the selection of empirical treatment. However, more patient data needs to be examined to guide the diagnosis and treatment.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were by the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Funding: *None*

Conflict of interest

The authors declare no conflict of interest.

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How to cite this article:
Ramazan Giden. *Evaluation of patients who had lumbar puncture in the emergency department. Ann Clin Anal Med 2023;14(3):212-217*

This study was approved by the Clinical Research Ethics Committee of Harran University (Date: 2021-06-21, No: HRU/12.12.14)